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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,829	05/17/2006	Hiroshi Kase	00005.001293.	5752

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EXAMINER	
PIHONAK, SARAH	
ART UNIT	PAPER NUMBER
4121	
MAIL DATE	DELIVERY MODE
03/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,829	KASE ET AL.	
	Examiner	Art Unit	
	SARAH PIHONAK	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14 and 15* is/are pending in the application.

4a) Of the above claim(s) *1-5,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8* is/are rejected.

7)☒ Claim(s) *9-12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 (national stage application) of PCT/JP04/18765, filed on 12/9/04. This application also claims foreign priority to Application No. 2003-410432, filed on 12/9/03.

Priority

This application has an effective filing date of 5/17/06. This application also claims foreign priority to Application No. 2003-410432. A certified copy of Application No. 2003-410432, filed on 12/9/03, has been received and filed, as well as a certified English translation of the International Application No. PCT/JP04/18765. The PCT/JP04/18765 application provides support to the instant claims in the application. As such, the priority date given to the instant claims is 12/9/03.

1. Claims 1-12, and 14-15 are pending.

2. Applicant's election of the invention of Group II, claims 6-12, in the reply filed on 3/10/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant also elected the species compound *(E)*-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methylxanthine, which is also known as KW 6002, in the reply filed on 3/10/09.

3. Claims 1-5, and 14-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no

allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/10/09.

4. Claims 6-12 were examined.

5. Claims 6-8 are rejected.

6. Claims 9-12 are objected to.

Claim Objections

7. Claims 9-12 are objected to under 37 CFR 1.75(c) as being in improper form because they are stated as being dependent claims of claims 6-8, and are therefore multiple dependent claims. See MPEP § 608.01(n). Accordingly, the claims 9-12 have not been further treated on the merits.

35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,727,259 patent in view of Kase, *Biosci., Biotechnol. Biochem.*, **65**, 1447-1457, 2001, and Middleton et. al., *Brain Res. Rev.*, **31**, 236-250, 2001, as evidenced by Graybiel, *Current Op. Neurobio.*, **5**, 733-741, 1995,.

11. Instant claim 6 cites a method for preventing and/or treating a higher brain dysfunction caused by brain injury comprising administration of an effective amount of the elected compound, *(E)*-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methylxanthine, also known as KW 6002. The US '259 patent discloses that KW 6002 is a therapeutic agent useful for treating neurodegenerative disorders, such as Alzheimer's disease, Huntington's chorea, brain ischemia, and other disorders (column 1, lines 25-29, column 3, Table 1, compound 1, and column 6, lines 41-48).

12. Instant claim 7 cites the method as stated in instant claim 6, and that the brain injury is due to aging. The US '259 patent teaches that the composition comprised of KW 6002 is effective for treating neurodegenerative disorders (column 1, lines 25-29, column 3, Table 1, and column 6, lines 41-48).

13. Instant claim 8 cites the method as stated in instant claim 6, and also, that the brain injury is due to a disorder resulting from a cerebrovascular accident. The US '259 patent teaches that the composition comprised of KW 6002 is effective for treating neurodegenerative disorders (column 1, lines 25-29, column 3, Table 1, and column 6, lines 41-48).

14. Regarding instant claim 6, the US '259 patent does not teach that KW 6002 would be a therapeutic agent for treating a higher brain dysfunction caused by brain injury.

15. Regarding instant claim 7, the US '259 patent does not teach that KW 6002 would be a therapeutic agent for treating a higher brain dysfunction caused by brain injury due to aging.

16. Regarding instant claim 8, the US '259 patent does not teach that KW 6002 would be a therapeutic agent for treating a brain injury due to a cerebrovascular accident.

17. Kase teaches that KW 6002 is a potent adenosine A2A receptor antagonist that has been shown to cause a significant reversal of motor disability associated with damage to the basal ganglia, as caused by administration of MPTP (1-methyl-4-phenyl-1,2,2,6-tetrahydropyridine) (p. 1448, right column, last paragraph).

18. Regarding instant claim 6, Kase does not teach that KW 6002 is a therapeutic agent to treat higher brain dysfunction associated with brain injury.

19. Regarding instant claim 7, Kase does not teach that KW 6002 is a therapeutic agent to treat higher brain dysfunction associated with brain injury caused by aging.

20. Regarding instant claim 8, Kase does not teach that KW 6002 is a therapeutic agent to treat higher brain dysfunction associated with brain injury caused by a cerebrovascular accident.

21. Middleton et. al. teaches that damage to the basal ganglia is associated with cognitive, sensory, and motor dysfunctions (p. 244, paragraphs 2 and 4).

22. Regarding instant claim 6, Middleton et. al. does not teach that KW 6002 is a therapeutic agent to treat higher brain dysfunction associated with brain injury.

23. Regarding instant claim 7, Middleton et. al. does not teach that KW 6002 is a therapeutic agent to treat higher brain dysfunction associated with brain injury caused by aging.

24. Regarding instant claim 8, Middleton et. al. does not teach that KW 6002 is a therapeutic agent to treat higher brain dysfunction associated with brain injury caused by a cerebrovascular accident.

25. It is known in the art that neurodegenerative disorders such as Alzheimer's disease and Huntington's chorea involve pathologies at the basal ganglia of the brain. The basal ganglia are a group of nuclei in the brain that are interconnected with the striatum, the globus pallidus, substantia nigra and subthalamus nucleus, as taught by Hase (p. 1449, left column, 1st paragraph). Brain ischemia due to cerebrovascular accidents such as stroke and cardiovascular infarction can also lead to defects in the basal ganglia. Physical traumatic injury to the brain can also cause injury to the basal ganglia. Middleton et. al. teaches that injury to the basal ganglia is associated with cognitive and motor skill deficits, as well as sensory dysfunction (p. 244, paragraphs 2 and 4). Graybiel teaches that the basal ganglia are associated with learning and memory (p. 734, right column, 2nd paragraph). Hase also teaches that KW 6002 is a

potent antagonist for adenosine A2A receptors in the basal ganglia (p. 1477, last paragraph), and that administration of KW 6002 in vivo led to an increase in locomotor activity, along with a significant decrease of motor disability, to subjects after administration of MPTP (1-methyl-4-phenyl-1,2,2,6-tetrahydropyridine) (p. 1448, right column, last paragraph). MPTP is known to cause lesions of the basal ganglia, and results in deficits associated with damage of the basal ganglia. Therefore, as KW 6002 is known to function as an antagonist of the adenosine A2A receptors of the basal ganglia, and has been shown to reverse motor disability, it would be expected that KW 6002 would also be effective at reversing motor disability associated with damage to the basal ganglia caused by other factors, such as neurodegenerative diseases, cardiovascular incidents, or physical trauma. Additionally, as the basal ganglia has been associated with learning and memory, as taught by Graybiel (p. 734, right column, 2nd paragraph), and Middleton et. al. (p. 244, paragraphs 2 and 4), it would have been expected at the time the invention was made that KW 6002 would be effective as a therapeutic agent to treat other impairments associated with damage or pathology to the basal ganglia, such as memory and learning. Therefore, while the US ‘259 patent, Middleton, Hase, and Graybiel do not individually teach all of the elements of instant claims 6-8 collectively, the references teach that KW 6002 would be useful as a therapeutic agent for the treatment of higher brain dysfunctions, such as memory and learning, caused by a brain injury to the basal ganglia. As such, it would have been prima facie obvious at the time the invention was made that KW 6002 could be used as a

therapeutic agent to treat higher brain dysfunctions resulting from brain injury, as the US '259 patent teaches that KW 6002 could be used to treat neurodegenerative disorders associated with pathology to the basal ganglia, such as Huntington's disease (column 1, lines 25-28, column 3, Table 1, compound 1, and column 6, lines 41-48), while Hase teaches that KW 6002 is effective at treating motor disability associated with damage to the basal ganglia (p. 1448, right column, last paragraph), and Middleton et. al. teaches that the basal ganglia are associated with motor activity, as well as cognitive functions (p. 244, paragraphs 2 and 4).

Double Patenting-Obviousness

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 6-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-3 of U.S. Patent No. 6,727,259. Although the conflicting claims are not identical, they are not patentably distinct from each other because they encompass the same scope of invention.

28. Instant claim 6 cites a method for preventing or treating higher brain dysfunction caused by brain injury, which comprises administration of an effective amount of the elected compound, KW 6002, to a patient in need of such treatment. Claim 2 of the US '259 patent discloses that KW 6002 is used to treat neurodegenerative disorders, with the exception of Parkinson's disease, but does not cite that KW 6002 is an agent to treat higher brain dysfunction associated

with brain injury. Claim 3 of the US '259 patent cites that KW 6002 is used to treat Alzheimer's disease, but does not cite that KW 6002 is an agent to treat higher brain dysfunction associated with brain injury.

29. Instant claim 7 cites the method as stated in instant claim 6, and also, that the brain injury is due to aging. Claim 2 of the US '259 patent cites a method of treating neurodegenerative disorders, except for Parkinson's disease, which comprises administration of an effective dose of the elected compound, KW 6002, but does not cite that KW 6002 is an agent used to treat higher brain dysfunction associated with a brain injury due to aging. Claim 3 of the US '259 patent cites that KW 6002 is used to treat Alzheimer's disease, but does not cite that KW 6002 is an agent to treat higher brain dysfunction associated with brain injury due to aging.

30. Instant claim 8 cites a method as stated in instant claim 6, and that the brain injury is due to a cerebrovascular accident. Claim 3 of the US '259 patent cites a method of treating Alzheimer's disease, which comprises administration of an effective dose of the elected compound, KW 6002, but does not cite that KW 6002 is an agent used to treat higher brain dysfunction associated with a cerebrovascular accident. Claim 2 of the US '259 patent discloses that KW 6002 is used to treat neurodegenerative disorders, with the exception of Parkinson's disease, but does not cite that KW 6002 is an agent to treat higher brain dysfunction associated with brain injury due to a cerebrovascular accident.

31. Kase teaches that KW 6002 is a potent adenosine A2A receptor antagonist that has been shown to cause a significant reversal of motor disability

associated with damage to the basal ganglia, as caused by administration of MPTP (1-methyl-4-phenyl-1,2,2,6-tetrahydropyridine) (p. 1448, right column, last paragraph).

32. Regarding instant claim 6, Kase does not teach that KW 6002 is a therapeutic agent used to treat higher brain dysfunction associated with brain injury.

33. Regarding instant claim 7, Kase does not teach that KW 6002 is a therapeutic agent used to treat higher brain dysfunction associated with a brain injury due to aging.

34. Regarding instant claim 8, Kase does not teach that KW 6002 is an agent used to treat a higher brain dysfunction associated with a brain injury caused by a cerebrovascular accident.

35. Middleton et. al. teaches that damage to the basal ganglia is associated with cognitive, sensory, and motor dysfunctions (p. 244, paragraphs 2 and 4).

36. Regarding instant claim 6, Middleton et. al. does not teach that KW 6002 is an agent used to treat higher brain dysfunction associated with brain injury.

37. Regarding instant claim 7, Middleton et. al. does not teach that KW 6002 is an agent used to treat higher brain dysfunction associated with a brain injury due to aging.

38. Regarding instant claim 8, Middleton et. al. does not teach that KW 6002 is an agent used to treat higher brain dysfunction associated with a brain injury due to a cerebrovascular accident.

39. Kase teaches that KW 6002 is a potent adenosine A2A antagonist that is effective at reducing motor disability associated with damage to the basal ganglia (p. 1448, right column, last paragraph). Middleton et. al. teaches that the basal ganglia are associated with cognitive, motor, and sensory functions (p. 244, paragraphs 2 and 4). It is known in the art that neurodegenerative disorders such as Alzheimer's disease and Huntington's disease are associated with pathologies in the basal ganglia. Claim 2 of the US '259 patent cites that KW 6002 is used to treat neurodegenerative disorders except Parkinson's disease, and claim 3 of the US '259 patent cites that KW 6002 is used to treat Alzheimer's disease. Brain injuries caused by cerebrovascular incidents, or physical trauma can also cause damage to the basal ganglia. Therefore, as KW 6002 is taught by Kase to reduce symptoms associated with damage to the basal ganglia, it would have been expected also to be effective at treating damage to the basal ganglia caused by brain injuries, whether by aging or physical trauma, in addition to damage caused by neurodegenerative disorders. Furthermore, as Middleton et. al. teaches that the basal ganglia is associated with cognitive and sensory functioning in addition to motor functions, it would have been expected that KW 6002 would also be effective at treating higher brain dysfunction as associated with cognitive disability, as Kase teaches that KW 6002 is effective at reducing symptoms associated with damage to the basal ganglia (p. 1448, right column, last paragraph). Therefore, it would have been prima facie obvious at the time the invention was made that, in addition to treating neurodegenerative disorders, KW 6002 would have been useful as an agent to treat higher brain dysfunction

associated with brain injury, as Kase teaches that KW 6002 is a potent agent for reducing symptoms associated with damage to the basal ganglia, while Middleton et. al. teaches that the basal ganglia are associated with higher brain functions such as cognition, motor, and sensory functioning. Therefore, claims 2 and 3 of the US '259 patent and instant claim 6 encompass the same inventive scope.

40. Regarding instant claim 7, brain injuries to the basal ganglia can be caused by cerebrovascular incidents, such as stroke and cardiovascular infarction. Cerebrovascular incidents are often associated with aging. In addition to treating neurodegenerative disorders, KW 6002 would have been useful as an agent to treat higher brain dysfunction associated with brain injury, as Kase teaches that KW 6002 is a potent agent for reducing symptoms associated with damage to the basal ganglia (p. 1448, right column, last paragraph), while Middleton et. al. teaches that the basal ganglia are associated with higher brain functions such as cognition, motor, and sensory functioning (p. 244, paragraphs 2 and 4). As cerebrovascular incidents, which cause damage to the basal ganglia, are associated with aging, claims 2 and 3 of the US '259 patent and instant claim 7 encompass the same inventive scope.

41. Regarding instant claim 8, brain injuries are also associated with cerebrovascular accidents. In addition to treating neurodegenerative disorders, KW 6002 would have been useful as an agent to treat higher brain dysfunction associated with brain injury, as Kase teaches that KW 6002 is a potent agent for reducing symptoms associated with damage to the basal ganglia (p. 1448, right

column, last paragraph), while Middleton et. al. teaches that the basal ganglia are associated with higher brain functions such as cognition, motor, and sensory functioning (p. 244, paragraphs 2 and 4). Therefore, claims 2 and 3 of the US '259 patent and instant claim 8 share the same inventive scope.

42. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Information Disclosure Statement

43. The information disclosure statement (IDS) submitted on 10/18/06 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 7:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571)272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/Patrick J. Nolan/
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